

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

**Application Number: 021042 and 021052**

**Trade Name: VIOXX TABLETS 12.5 MG and 25 MG,  
VIOXX ORAL SUSPENSION 12.5 MG/mL and 25MG/mL**

**Generic Name: ROFECOXIB TABLETS AND ORAL  
SUSPENSION**

**Sponsor: MERCK RESEARCH LABORATORIES**

**Approval Date: 05/20/99**

**INDICATION(s): FOR RELIEF OF SIGNS AND  
SYMPTOMS OF OSTEOARTHRITIS, THE  
MANAGEMENT OF ACUTE PAIN, AND THE  
TREATMENT OF PRIMARY DYSMENORRHEA.**

# **CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION for:    021042 and 021052**

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	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
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Final Printed Labeling	X			
Medical Review(s)	X			
Chemistry Review(s)	X			
EA/FONSI	X			
Pharmacology Review(s)	X			
Statistical Review(s)	X			
Microbiology Review(s)			X	
Clinical Pharmacology Biopharmaceutics Review(s)	X			
Bioequivalence Review(s)			X	
Administrative Document(s)/ Correspondence	X			

NDA 21-042

Merck Research Laboratories  
Attention: Robert E. Silverman, M.D., Ph.D.  
Senior Director, Regulatory Affairs  
Sumneytown Pike  
P.O. Box 4, BLA-20  
West Point, Pennsylvania 19486

Dear Dr. Silverman:

Please refer to your new drug application (NDA) dated November 23, 1998, received November 23, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vioxx (rofecoxib tablets) Tablets 12.5 mg and 25 mg.

We acknowledge receipt of your submissions dated November 23 and 25; December 10, 16 (two), 18 (three), 22, and 23, 1998; January 5, 7 (two), 12 (two), 13, 18, 19, 26, and 27 (two); February 1, 2 (two), 5 (three), 9 (two), 11, 18 (three), 19, and 23; March 4 (two), 5 (five), 8, 9 (two), 10 (eight), 12 (two), 15 (three), 16 (three), 17, 18 (three), 19 (two), 22 (two), 23 (five), 25 (two), and 31 (four); April 1 (two), 5 (two), 6, 12, 13 (two), 15 (two), 16, 19 (two), 26, and 30; and May 4, 5, 6 (three), 7 (two), 10, 11 (two), 12, 13, 14, 17, 18, and 19, 1999.

This new drug application provides for the use of Vioxx (rofecoxib tablets) Tablets 12.5 mg and 25 mg for relief of the signs and symptoms of osteoarthritis, the management of acute pain, and the treatment of primary dysmenorrhea.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-042." Approval of this submission by FDA is not required before the labeling is used.

If additional information relating to the safety or effectiveness of this drug becomes available, revision

of the labeling may be required.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please note that any advertising and/or promotional activity of this product will be considered false and/or misleading under Section 502 of the Act if it presents suggestions or representations that COX-2 selectivity confers on the product any claims of safety beyond what has been demonstrated in clinical studies and presented in the approved labeling. Additionally, promotional activities that make or imply comparative claims about the frequency of clinically serious gastrointestinal (GI) events compared to groups of NSAIDs or specific NSAIDs will be considered false and/or misleading without differences having been demonstrated in adequate, well-controlled studies. Finally, any promotional use of the endoscopic data without the qualifying explanations of that data found in the approved labeling (paragraph beginning on line 231 in the enclosed label text, and the sentence on lines 209 and 210) will be considered false and/or misleading. If you have any questions or concerns about this matter please contact the Center for Drug Evaluation and Research's Division of Drug Marketing, Advertising and Communications.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We are deferring submission of your pediatric studies until December 3, 2000. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at [www.fda.gov/cder/pediatric](http://www.fda.gov/cder/pediatric)) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. If you do not submit a Proposed Pediatric Study Request within 120 days from the date of this letter, we will presume that you are not interested in obtaining pediatric exclusivity [NOTE: You should still submit a pediatric drug development plan.] and we will notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity.

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Sandra N. Cook, Project Manager, at (301) 827-2090.

Sincerely,  
**/S/**

Robert J. DeLap, M.D., Ph.D.  
Director  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

Enclosure

APPEARS THIS WAY  
ON ORIGINAL



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

NDA 21-052

Food and Drug Administration  
Rockville MD 20857

Merck Research Laboratories  
Attention: Robert E. Silverman, M.D., Ph.D.  
Senior Director, Regulatory Affairs  
Sunneytown Pike  
P.O. Box 4, BLA-20  
West Point, Pennsylvania 19486

MAY 20 1999

Dear Dr. Silverman:

Please refer to your new drug application (NDA) dated November 23, 1998, received November 23, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vioxx (rofecoxib oral suspension) Oral Suspension 12.5 mg/mL and 25 mg/mL.

We acknowledge receipt of your submissions dated November 23 and 25; December 23, 1998; January 7; February 5 and 19; March 5, 23 (two), 25, and 29; and May 12, 14 (two), 18, and 19, 1999.

This new drug application provides for the use of Vioxx (rofecoxib oral suspension) Oral Suspension 12.5 mg/mL and 25 mg/mL for relief of the signs and symptoms of osteoarthritis, the management of acute pain, and the treatment of primary dysmenorrhea.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-052." Approval of this submission by FDA is not required before the labeling is used.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please note that any advertising and/or promotional activity of this product will be considered false and/or misleading under Section 502 of the Act if it presents suggestions or representations that COX-2 selectivity confers on the product any claims of safety beyond what has been demonstrated in clinical studies and presented in the approved labeling. Additionally, promotional activities that make or imply comparative claims about the frequency of clinically serious gastrointestinal (GI) events compared to groups of NSAIDs or specific NSAIDs will be considered false and/or misleading without differences having been demonstrated in adequate, well-controlled studies. Finally, any promotional use of the endoscopic data without the qualifying explanations of that data found in the approved labeling (paragraph beginning on line 231 in the enclosed label text, and the sentence on lines 209 and 210) will be considered false and/or misleading. If you have any questions or concerns about this matter please contact the Center for Drug Evaluation and Research's Division of Drug Marketing, Advertising and Communications.

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NDA 21-052

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at [www.fda.gov/cder/pediatric](http://www.fda.gov/cder/pediatric)) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. If you do not submit a Proposed Pediatric Study Request within 120 days from the date of this letter, we will presume that you are not interested in obtaining pediatric exclusivity [NOTE: You should still submit a pediatric drug development plan.] and we will notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity.

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Sincerely,

/S/

Robert J. DeLap, M.D., Ph.D.

Director

Office of Drug Evaluation V

Center for Drug Evaluation and Research

Enclosure

APPEARS THIS WAY  
ON ORIGINAL